Disease Name — Beta-ketothiolase deficiency

Alternate name(s)	Alpha-methylacetoacetic aciduria, 2-methyl-3-hydroxybutyric academi, Mitochondrial acetoacetyl-CoA thiolase deficiency, MAT deficiency, T2 deficiency, 3-oxothiolase deficiency, 3-ketothiolase deficiency, 3-KTD deficiency
Acronym	BKD
Disease Classification	Organic Acid Disorder
Variants	No, but there is considerable clinical heterogeneity
Variant name	N/A
Symptom onset	Late infancy or childhood. Mean age at presentation is 15 months (range 3 days to 48 months). There are documented cases of asymptomatic patients with enzyme deficiency. Frequency of decompensation attacks falls with age and is uncommon after the age of 10.
Symptoms	Symptoms include intermittent episodes of severe metabolic acidosis and ketosis accompanied by vomiting (often hematemesis), diarrhea and coma that may progress to death. There is great clinical heterogeneity between patients. Infancy is the period of highest risk for decompensation. Death or neurologic complications can occur. Neurologic damage includes striatal necrosis of the basal ganglia, dystonia and/or mental retardation. Other symptoms include cardiomyopathy, prolonged QT interval, neutropenia, thrombocytopenia, poor weight gain, renal failure and short stature. If neurologically intact, patients are normal between episodes.
Natural history without treatment	Clinical outcome varies widely with a few patients suffering severe psychomotor retardation or death as a result of their initial attack and others with normal development and no episodes of acidosis.
Natural history with treatment	Despite severe recurrent attacks, appropriate supportive care can result in normal development.
Treatment	Avoidance of fasting. Bicarbonate therapy and intravenous glucose in acute crises. Possible protein restriction. Consider carnitine supplementation.
Other	N/A
Physical phenotype	No dysmorphisms
Inheritance	Autosomal recessive
General population incidence	unknown
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	Converts 2-methylacetoacetyl-CoA to propionyl-CoA and acetyl-CoA.
Enzyme Function	Catalyzes the decarboxylation of oxoacids.
Missing Enzyme	Mitochondrial acetoacetyl-CoA thiolase enzyme
Metabolite changes	Increased urinary excretion of 2-methyl-3-hydroxybutyric acid, 2-methylacetoacetic acid, tiglylglycine, 2-butanone, and ketone bodies (acetoacetic acid, 3-hydroxybutyric acid).
Gene	ACAT1
Gene location	11q22.3-q23.1
DNA testing available	Not in US. Sequencing of gene on a research basis.
DNA testing detail	No common mutation known
Prenatal testing	Enzyme analysis in amniocytes or CVS tissue. If mutations have been identified, DNA testing is possible.
MS/MS Profile	C5:1 tiglycarnitine – elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203750
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org